

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the present amendment and following remarks. Claims 1- 4, 19 and 21 were previously pending and under consideration. By this amendment, claims 1-4 are cancelled, and claims 19 and 21 are amended to more clearly recite certain aspects of the invention. It is urged that support for the above amendments can be found throughout the specification as originally filed and that none of the amendments constitute new matter. This amendment is not to be construed as acquiescence to any rejection and is made without prejudice to the prosecution of any subject matter modified by the amendment in a related divisional, continuation, or continuation-in-part application.

WITHDRAWAL OF REJECTION UNDER 35 U.S.C. § 101

Applicants wish to thank the Examiner for withdrawing the rejection under 35 U.S.C. § 101.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 2 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. More specifically, the Action asserts that the term "small" renders claim 2 indefinite, since the term is not defined by the claim or in the specification, and, therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Applicants respectfully traverse this basis of rejection and submit that the meaning of the term "small," in the context of a "small organic molecule," as recited in claim 2, would be readily understood by the skilled artisan and, therefore, adequately points out and distinctly claims the subject matter, as required under 35 U.S.C. § 112, second paragraph. Nonetheless, without acquiescence and solely to expedite prosecution, claim 2 has been cancelled, thereby obviating this basis of rejection. Applicants respectfully request that this basis of rejection be withdrawn.

Claims 1-4, 19 and 21 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Action asserts that the metes and bound of the term "directed to" cannot be readily ascertained.

Applicants respectfully traverse this basis of rejection and submit that the skilled artisan would understand the meaning of the term "directed to" in the context of the claimed invention. Without acquiescence, however, claims 1-4 have been cancelled, and claim 21 has been amended to recite "binds to" instead of "directed to." Support for monoclonal antibodies that bind to a vitamin B<sub>12</sub> binding site on TcII is provided throughout the specification, *e.g.*, page 17, lines 26-33, and Examples 8-12. Applicants submit that the skilled artisan would readily understand the scope of the claimed monoclonal antibodies that bind to a vitamin B<sub>12</sub> binding site on TcII and, therefore, respectfully request that this basis of rejection is reconsidered and withdrawn.

#### REJECTIONS UNDER 35 U.S.C. § 102(B)

Claims 1, 2, 3, 4 and 19 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Marcoullis *et al.* The Action asserts that that Marcoullis *et al.* teach an IgG fraction that neutralized the total unsaturated vitamin B<sub>12</sub> binding capacity, suggesting that the IgG fraction contained antibodies that bind TcII and neutralize the binding of vitamin B<sub>12</sub>. The Action further asserts that these antibodies necessarily possess the functions recited in the claims.

Applicants respectfully traverse this basis of rejection and maintain their position that Marcoullis *et al.* fails to disclose isolated antibodies directed to TcII. Instead, Marcoullis *et al.* describe an IgG fraction derived from a patient, which necessarily includes a large number of different antibodies, many or most of which are not directed against transcobalamin. However, without acquiescence to this basis of rejection, claims 1-4 have been cancelled and claim 19 has been amended to properly reflect dependency, thereby obviating this basis of rejection. Accordingly, Applicants respectfully request that this basis of rejection be withdrawn.

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Shimizu *et al.* Specifically, the Action alleges that Shimizu *et al.* teaches the compound, methyl-B<sub>12</sub>, which has an antitumor effect. The Action therefore concludes that methyl-B<sub>12</sub> meets the claimed structural and functional limitations of a claimed small organic molecule. Applicants maintain their view that Shimizu *et al.* fails to teach or even suggest that the observed anti-tumor effect may be related to methyl-B<sub>12</sub> inhibiting cellular uptake of vitamin B<sub>12</sub>. Rather, Shimizu *et al.* merely shows that methyl-B<sub>12</sub> is capable of exerting an antitumor

effect by stimulating the immune response, as demonstrated by methyl-B<sub>12</sub> promotion of mitogen-stimulated splenic lymphocyte blastoformation. Nonetheless, without acquiescence, claims 1 and 2 have been cancelled, thereby obviating this basis of rejection. Applicants respectfully request that this basis of rejection be properly withdrawn.

Claims 1-4, 19 and 21 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Carmel *et al.* The Action asserts that Carmel *et al.* discloses a monoclonal antibody that binds to human TcII, inhibits TcII-mediated uptake of cobalamin by K562 cells, and is necessarily a growth inhibitory agent as claimed.

Applicants respectfully traverse this basis of rejection. Applicants submit that Carmel *et al.* fails to disclose an isolated growth blocking agent that binds to a vitamin B<sub>12</sub> binding site on TcII, as presently recited in claim 19. As stated in the abstract of Carmel *et al.*, “[n]either of the two antibodies was directed at the cobalamin-binding site of TC II.” Accordingly, Applicants submit that remaining claims 19 and 21 are not anticipated by Carmel *et al.* and respectfully request reconsideration of this basis of rejection.

#### REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, NEW MATTER

Claims 1-4, 19 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter that was not adequately described in the specification. More specifically, the Action asserts that the specification as originally filed does not support the genus of growth inhibitory agents generically directed to TcII.

Applicants respectfully traverse this basis of rejection and submit that the skilled artisan would readily appreciate that the invention described in the specification as originally filed encompasses growth inhibitory agents directed to any region of TcII, based upon the disclosure in the specification of growth inhibitory reagents targeted to a variety of different regions of TcII. Without acquiescence, however, claims 1-4 have been cancelled and claim 21 amended to recite that the growth inhibitory agent bind to the vitamin B<sub>12</sub> binding site on TcII. Applicants submit that growth inhibitory reagents that bind to the vitamin B<sub>12</sub> binding site on TcII are disclosed in the specification and claims as originally filed, *e.g.*, page 17, lines 26-27, and respectfully request reconsideration and withdrawal of this basis of rejection.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-4 and 19 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not adequately described in the specification. More specifically, the Action asserts that the specification fails to provide written description of small organic molecules, polyclonal antibodies or peptides that are growth blocking agents directed to TcII and capable of inhibiting cellular uptake of vitamin B<sub>12</sub>. The Action further asserts that the description of monoclonal antibodies possessing the functional characteristics recited in the claims does not adequately support claims to the claimed genus of growth blocking agents, which includes small organic molecules, polyclonal antibodies and peptides.

Applicants respectfully traverse this basis of rejection and submit that the instant specification provides sufficient identifying characteristics to demonstrate to the skilled artisan that Applicants were in possession of the claimed invention at the time of filing the application. Applicants have provided at least two distinct and readily ascertainable functional characteristics by which the skilled artisan can easily recognize a claimed growth blocking agent, including the first identifying characteristic that the agent binds to a vitamin B<sub>12</sub> binding site on TcII, and the second identifying characteristic that the agent is capable of inhibiting the cellular uptake of vitamin B<sub>12</sub>. Nonetheless, without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 1-4 have been cancelled and claim 19 has been amended to no longer refer to the cancelled claims. Accordingly, Applicants respectfully submit that this basis of rejection has been obviated and request that it be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

Claims 1-4 and 19 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter not adequately enabled by the instant specification. The Action asserts that the specification fails to teach the skilled artisan how to make or use the full scope of the claimed invention without undue experimentation.

Applicants respectfully traverse this basis of rejection and submit that the specification adequately teaches the skilled artisan how to make and use the claimed invention. Applicants further submit that the production and screening of growth blocking agents directed to a vitamin B<sub>12</sub> binding site on TcII and capable of inhibiting cellular uptake of vitamin B<sub>12</sub> would

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require merely routine methods and assays and is, therefore, fully enabled by the instant specification. Nonetheless, without acquiescence to this basis of rejection and solely to expedite prosecution of the instant application, claims 1-4 have been cancelled and claim 19 has been amended to no longer refer to the cancelled claims. Accordingly, Applicants respectfully submit that this basis of rejection has been obviated and request that it be withdrawn.

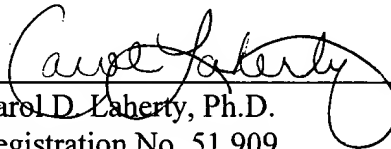
The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

A. Charles Morgan, Jr. et al.

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